RAMA UNIVERSITY

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FACULTY OF NURSING

Chapter-01

IMMUNITY

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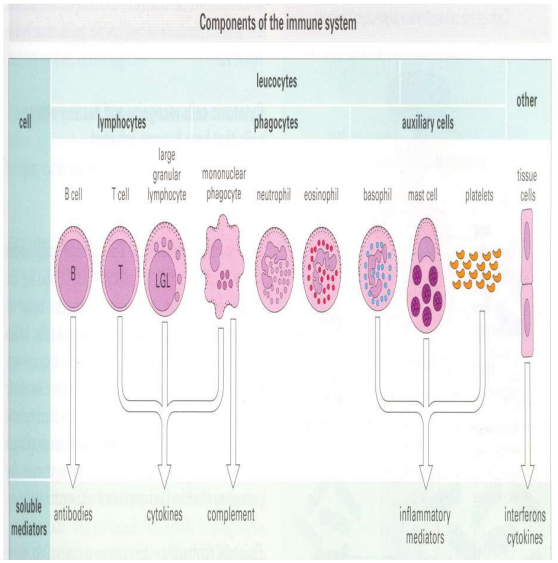
Content:

IMMUNITY
DEFINITION

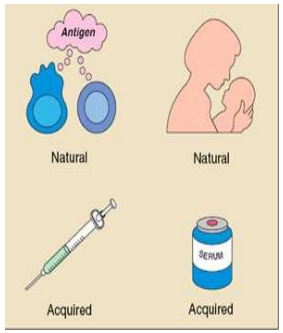
- Resistance acquired by a host towards injury caused by microorganisms and their products.

- Protection against the infectious diseases is only one of the consequences of the immune response, which entirely is concerned with the reaction of the body against any foreign antigen.


Components of the immune system
cell
leucocytes
other
lymphocytes
phagocytes
auxiliary cells
B cell
T cell
large granular lymphocyte
mononuclear phagocyte
neutrophil
eosinophil
basophil
mast cell
platelets
tissue cells
B
T
LGL
soluble mediators
antibodies
cytokines
complement
inflammatory mediators
interferons cytokines

TYPES OF IMMUNITY:

- Innate immunity :
  - a. Nonspecific
    - Species
    - Racial
    - Individual
  - b. Specific
- Adaptive Immunity:
  - a. Active :
    - Natural
    - Artificial
  - b. Passive:
    - Natural
    - Artificial



Innate immunity:

Resistance to infection which an individual possesses by virtue of his genetic and constitutional makeup

Not affected by prior contact with microorganisms or immunization

a. Non specific :

Indicate a degree of resistance to infections in general

b. Specific:

Resistance to a particular pathogen is concerned.

Innate Immunity:

1. Species immunity:

Resistance to pathogen, shown by all members of a particular species.

E.g. *anthracis* infects human beings but not chickens

2. Racial Immunity:

Within a species, different races may show difference in susceptibility to infections.

E.g. Genetic resistance *Plasmodium falciparum* malaria resistance in Africa

3. Individual – immunity

Resistance to infection varies with different individuals of same race and species

E.g.. Homozygous twins exhibit similar resistance susceptibility to leprosy and Tuberculosis such correction is not seen in heterozygous twins.

Factors influencing innate immunity

1. Age :

In foetus immune system is immature, in old age there is gradual waning of immune system

E.g. Polio infection , and Chickenpox highly severe in adu

2. Hormonal :

Enhance suseptability to infection such as

E.g. Diabetes mellitus

- Hypothyroidism in adults
- Adrenal dysfunction

3. Nutrition

E.g. Malnutrition predisposes to bacterial infection.

- Both humoral and cell mediated immune responses a[illegible] malnutrition.

Mechanism of innate immunity:

1. Epithelial surface:

a. Skin:

- It acts as a machanical barrier to microorganisms and provide bactericidal

  secretions
- Resident microflora of skin and mucous membrane suface help

  to prevent colonisation by pathogens
- Altertation of normal resident flora may lead to invasion by extraneous

  microbes and thus causing serious disease.
- e.g Clostridial enterocoloitis fallowing oral antibiotics

b. Resiratory tract:

- Inhaled particals are arrested in the nasal passage on the moist mucous membrane surface.
- Mucous membrane acts as a trapping mechanism hair like cilia propels the particals towards pharynx where its swallowed or coughed out.
- Cough reflex acts as a defence mechanism

c. Intestinal tract:

- Mouth possesses saliva which has a inhibitory effect on many microorganisms some bacteria are destroyed by acidic pH of gastric juices
- Normal bacterial flora of intestine exerts a protective colonisation of pathogenic bacteria

d. conjunctiva:

- Tears (contain lysosyme which has anti bacterial property) helps in flusing away bacteria and other dust particals.

e. Genitourinary tract:

- Flusing action of urine eliminates bacteria from uretar

2. Antibacterial substance:

- Nonspecific antibacterial substance present in the blood and tissue
- Substance like properiden, complement, lysosyme, betalysin, basic polypeptide and interferon which have antiviral activity.
- Complement system plays an important role in destruction of pathogenic microorganisms that invade blood and tissue.

3. **Cellular factor :**

- When infection cross the barrier of epithelial suface, tissue factor come into play for defence.
- Exudate inflammatory reaction occurs by accumulation of phagocytes at the site of infection and deposition of fibrin which entangles the organisms to act as a barrier to spread of infection. Phagocytic cells ingest these organisms and destroy them.

Phagocytic cells are classified as:

i) Microphages e.g. polymorphomuclera leucocytes (neutrophils)

ii) Macrophages e.g mononuclear phagocytic cells

Phagocytic action are divided into 4 stages:

i) Chemotaxis:

Phagocytes reach the site of infection attracted by chemotactic substances

ii) Attachment:

Infective agent gets attached to phagocytic membrane

iii) Ingestion:

Phagoctes engulf the infective material into vacule

Membrane of phagosome fuses with lysosomes to form a phagolysosome.

iv) Intracellular killing:

Most bacteria are destroyed by phagolysosomes by hydrocytic enzymes of lysosomes Natural killer cells play a important role in non specific defence against viral infections and tumour.

4. Inflammation:

Inflammation occurs as a result of tissue injury or irritation, initiated by entry of pathogens or other irritants.

It's a nonspecific defence mechanism.

Inflammtion leads to vasodilatation, increased vascular permeability

and cellular infiltration.

Microorganisms are phagocytosed and destroyed due to increased vascular permeability, which helps to dilute the toxic products present. Fibrin barrier is laid to wall off site of infection

5. Fever:

Rise of temperature fallowing infection is a natural defence mechanism. It destroyes the infecting organisms.

Fewer also stimulates the production of interferon which helps in recovery from viral infection.

6. Acute phase protein:

Fallowing infection or injury, there is a sudden increase in plasma concentration of certain proteins, called acute phase proteins This include c-reactive protein, mannose binding protein etc

CRP and acute phase protein activate alternative pathway of complement. This is caused to prevent tissue injury and promote repair of inflammtion lesions.

ADAPTIVE IMMUNITY

- This is inducible and develops slowly than the innate response.
- This is specific kind of immunity and has memory, therefore providing long term protection.
- This occurs with contact of foreign particle

Adaptive immunity is often sub-divided into two major types depending on how the immunity was introduced.

I. **Naturally acquired immunity** occurs through contact with a disease causing agent, when the contact was not deliberate

II. **Artificially acquired immunity** develops only through deliberate actions such as vaccination

Mechanism:

Active immunity response stimulates both humoral and cell mediated immunity usually parallel

i) Humoral immunity:

It's a antibody mediated immunity

It depends on the synthesis of antibodies by plasma cells, the cells produce specific circulating antibody which combine specifically with the antigens and modify their activity.

Modified activity is done by lysis of antigen molecules their toxin may be neutralised or in the form of removal of antigen by phagocytosis.

ii) Cell mediated immunity:

Depends on T- lymohocytes

Cell mediated immunity by sensitised T lymphocytes helps in resistance to chronic bacterial infections in chronic infection, organisms can multiply and survive in phagolysosomes and In viral infections.

TYPES OF ADAPTIVE IMMUNITY

Active immunity :

a. Naturally acquired active immunity occurs when the person is exposed to a live pathogen, develops the disease, and becomes immune as a result of the primary immune response.

b. Artificially acquired active immunity can be induced by a vaccine, a substance that contains the antigen. A vaccine stimulates a primary response against the antigen without causing symptoms of the disease.

Vaccine :

Live vaccine: BCG for tuberculosis, Sabin vaccine for poliomylitis Killed vaccine: Hepatitis B vaccine, non-neural vaccine for rabies

Bacterial product: Tetanus toxoid vaccine, Deptheria toxoid for deptheria

Passive immunity:

a. Artificially acquired passive immunity is a short-term immunization by the injection of antibodies, such as gamma globulin, that are not produced by the recipient's cells.

a. Naturally acquired passive immunity occurs during pregnancy, in which certain antibodies are passed from the maternal into the fetal bloodstream

Active immunity

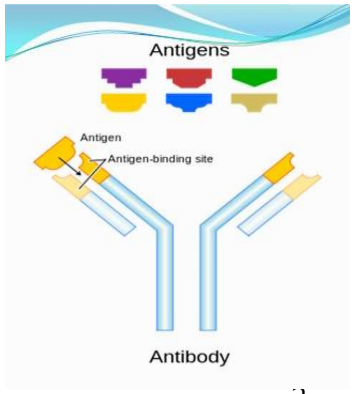
- Induced by infection
- Long lasting and effective protection
- Effective only after lag period
- Exposure leads to immediate maximal response
- Immunological memeory present
- Negative phase may occur
- Not applicable to immunodeficient person
- Used for prophylaxis to increase body resistance e.g BCG vaccine

Passive immunity

- Conferred by administration of ready made antibodies.
- Short lived and less effective
- Effective immediately
- Lag time between exposure and maximal response
- No immunological memory
- No negative phase
- Applicable to immunodeficient person
- Used for treatment of acute infection

ANTIGEN

An antigen is a molecule that induces an immune response in the body.



Origin of antigen

Exogenous antigens

- Antigens that have entered the body from the outside.

E.g. By inhalation, ingestion, or injection.

Endogenous antigens

- Antigens that have been generated within previously normal cells as a result of normal cell metabolism, or because of viral or intracellular bacterial infection

- An autoantigen is usually a normal protein or complex of proteins (and sometimes DNA or RNA) that is recognized by the immune system of patients suffering from a specific autoimmune disease.
- These antigens should, under normal conditions, not be the target of the immune system, but, due to mainly genetic and environmental factors, the normal immunological tolerance for such an antigen has been lost in these patients.

Immunogen

- An **immunogen** is in analogy to the antigen,
- It is a substance (or a mixture of substances) that is able to provoke an immune response if injected to the body.
- An immunogen is able to **initiate** an innate immune response first, later leading to the activation of the adaptive immune response, whereas an antigen is able to **bind** the highly variable immunoreceptor products (b-cell receptor or t-cell receptor) once these have been produced.

- **Immunogenicity** is the ability to induce a humoral and/or cell-mediated immune response
- **Antigenicity** is the ability to combine specifically with the final products of the immune response (i.e. Secreted antibodies and/or surface receptors on t-cells). Although all molecules that have the property of immunogenicity also have the property of antigenicity, the reverse is not true

Antigen(ic) specificity

Is the ability of the host cells to recognize an antigen specifically as a unique molecular entity and distinguish it from another with exquisite precision. Antigen specificity is primarily due to the side-chain conformations of the antigen.

Hapten

Is a small molecule that can elicit an immune response only when attached to a large carrier such as a protein; the carrier may be one that also does not elicit an immune response by itself.

Epitope:

The portion of an antigen that recognize and bound by antibody and also called antigenic determinant.

- An **antigen-presenting cell** (**APC**) or **accessory cell** is a cell that displays foreign antigens complexed with major histocompatibility complexes (MHC's) on their surfaces; this process is known as antigen presentation.
- T-cells may recognize these complexes using their T-cell receptors (TCRs). These cells process antigens and present them to T-cells.

Eg.

- Dendritic cell,
- Macrophages,
- B cell,
- Epithelial cells,
- Fibroblast

Antibody : immunoglobulin

Immunoglobulin is a glycoprotein that is made in response to an antigen and can recognize and bind to the antigen that caused its production.

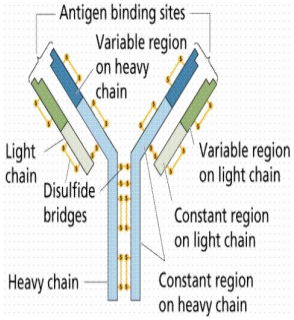
- Are gamma globulins
- Synthesized by plasma cells
- Constitute 25-30 % of total serum proteins
- Antibodies are present in serum, tissue fluids and mucosal surfaces.
- All antibodies are immunoglobulins, but all immunoglobulins may not be antibodies

ANTIBODY STRUCTURE

An antibody (Ab), also known as an immunoglobulin (Ig)

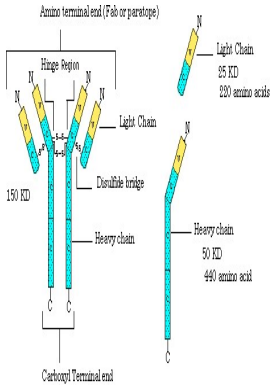
It's a large Y-shape protein produced by B cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses.

The antibody recognizes a unique part of the foreign target, called an antigen.

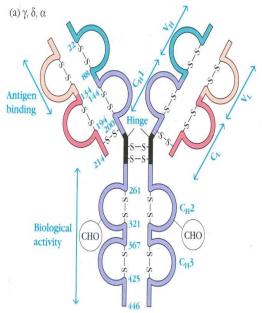


Basic structure

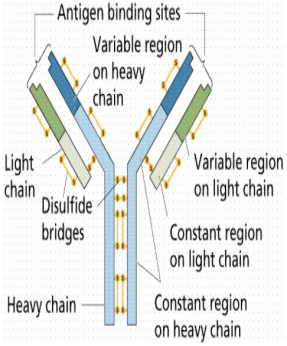
- Composed of 4 polypeptide chains.
- 2 identical light and 2 identical heavy chains
- Linked by disulphide bonds
- Light chains similar in all immunoglobulins
- Light chains occur in 2 varieties kappa and lambda
- Light and Heavy chains are subdivided into variable and constant region.
- Each heavy and light chain contains amino terminal in variable region, carboxyl terminal in constant region



- Heavy chains are structurally and antigenically distinct for each class
- Each immunoglobulin peptide chain has intra chain disulphide bonds- form loops
- Each loop is compactly folded to form a globular structure-domain
- Light chain contains a single variable domain (VL) and a single constant domain (CL).
- Heavy chain contains one variable domain (VH) and 3 constant domains (CH1, CH2, CH3)
- Hinge region is the segment in heavy chain - between CH1, CH2



- Each tip of the "Y" of an antibody contains a paratope that is specific for one particular epitope on an antigen, allowing these two structures to bind together with precision.
- Using this binding mechanism, an antibody can *tag* a microbe or an infected cell for attack by other parts of the immune system, or can neutralize its target directly.
- The production of antibodies is the main function of the humoral immune system.
- Antibodies are secreted by a type of white blood cell called a plasma cell.



- Antibodies can occur in two physical forms

1. Soluble form that is secreted from the cell,

2. Membrane-bound form

That is attached to the surface of a B cell and is referred to as the B cell receptor (BCR).

The BCR is only found on the surface of B cells

Facilitates the activation of these cells and their subsequent

differentiation into either antibody factories called plasma cells or memory B cells

That will survive in the body and remember that same antigen so the B cells can respond faster upon future exposure.

Classification

- Based on structure and antigenic nature of H chain the immunoglobulins are classified into 5 classes.
- Ig G- (gamma)
- Ig A- *(alpha)*
- *Ig M- (mu)*
- *Ig D- (delta)*
- *Ig E - (epsilon)*

Functions of Different Antibodies

1.IgA plays a role in localized defense mechanism in external secretions like tear

2. IgD is involved in recognition of the antigen by B lymphocytes

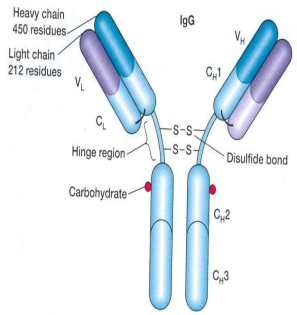
3. IgE is involved in allergic reactions

4. IgG is responsible for complement fixation

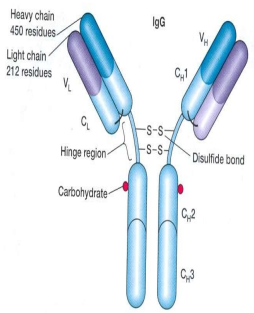
5. IgM is also responsible for complement fixation.

Immunoglobulin G
(Ig G)

- Most abundant class in serum
- Constitutes 80% total immunoglobulin
- Present in blood, plasma and tissue fluids
- Contains less carbohydrate than other immunoglobulins
- It has a half life of 23 days: the longest of all of the immunoglobulin isotopes

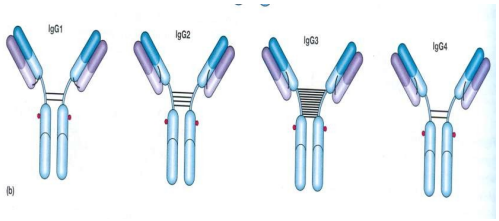


- Crosses placenta and provide natural immunity to fetus and neonate at birth
- Acts against bacteria and viruses by opsonizing
- Neutralize toxin
- Activate complement by classical pathway
- Catabolism of IgG is unique in that it varies with its serum concentration



Sub classes of Ig G

Ig G1, Ig G2, Ig G3, Ig G4.

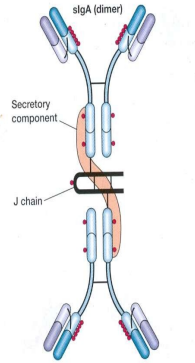


Biological function of subclasses

- IgG1, IgG3, IgG4 – cross placenta and protect fetus
- IgG3 activates complement
- IgG1 and IgG3 binds to Fc receptor on phagocytic cells, monocytes and macrophages and mediate opsinization.

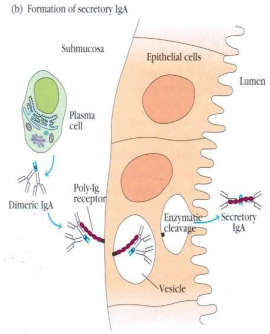
Immunoglobulin A (Ig A)

- Constitutes 10-15 % of total immunoglobulins
- Present in milk, saliva, tears, mucous of respiratory tract, digestive tract and genitourinary tract.
- In serum exist as monomer
- In external secretions exist as dimer called secretory Immunoglobulin.
- Has 'J' chain and secretory piece.
- Half life: 6-8 days



Formation of secretory Ig A

- Dimeric Ig A binds to the receptor on the surface of the epithelial cells -endocytosed and transported across the cell to the luminal surface
- After reaching the surface, the poly-Ig receptor is cleaved
- The portion of the receptor that remains attached to the Ig A dimer – secretory component
- Secretory piece protects Ig A from digestive enzymes and denaturation by bacterial proteases

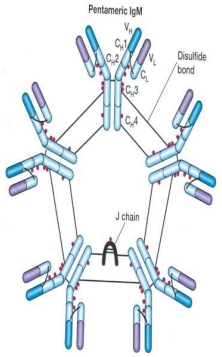


Functions

- Provides local immunity.
- Secretory Ig A binds to surface antigens of microorganism and prevent its attachment and invasion of the mucosal surfaces of respiratory and digestive tract- immune elimination.
- Secretory IgA provides important line of defense against *salmonella*, *Vibrio cholerae*, *N. gonorrhoeae*, influenza virus and poliovirus.
- Secretory IgA present in breast milk protects newborn during first months of life.
- Activates complement by the alternative pathway
- Promotes phagocytosis and intracellular killing of microorganisms

Immunoglobulin M (Ig M)

- Accounts for 5-10% of total serum proteins
- Polymer of five monomeric units (pentamer)
- Held together by disulfide bonds and ‘J’ chain
- Mol. Wt. of 900,000-10,00,000 (millionaire molecule)
- Half life: 5 days



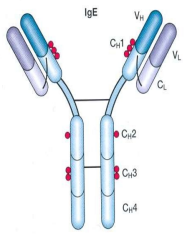
- Most of IgM (80%) present intravascularly
- Present in low concentration in intercellular tissue fluids
- Cannot cross placenta
- Presence of IgM antibody in serum of newborn indicate congenital infection.
- Earliest immunoglobulin to be synthesized by fetus (20 weeks)
- First immunoglobulin to be produced in primary response to antigen
- Relatively short-lived hence it's demonstration in the serum indicates recent infection
- Monomeric IgM appears on the surface of unstimulated B lymphocytes and act as receptors for antigens

Functions

- It agglutinates bacteria
- Activates complement by classical pathway
- Causes opsonization and immune hemolysis
- Believed to be responsible for protection against blood invasion by microorganisms

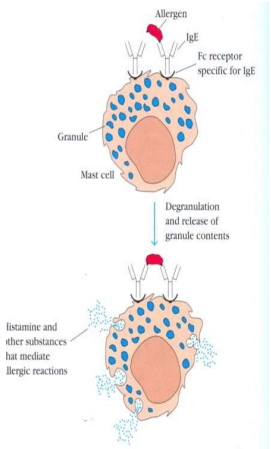
Immunoglobulin E
(Ig E)

- Structure is similar to Ig G
- Has 4 constant region domains.
- Mol. Wt. 1,90,000
- Half life: 2 days
- Heat labile (inactivated at 56^0C in 1 hour)
- Normal serum concentration 0.3 ug/ml
- Mostly present extra cellularly
- Does not cross placenta



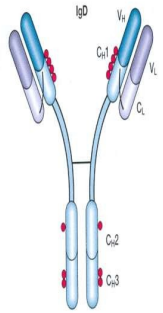
- Produced in the lining of respiratory and intestinal tract
- Known as regain antibody
- Does not activate complement nor agglutinate antigens
- Binds to the Fc receptors on the membranes of blood basophils and tissue mast cells
- Mediates immediate hypersensitivity reaction and P.K. reaction
- Responsible for symptoms of anaphylactic shock, hay fever and asthma.
- Play a role in immunity against helminthic parasites

- IgE binds to Fc receptors on the membrane of blood basophils and tissue mast cells.
- When two IgE molecules on the surface of these cells are cross linked by binding of the same antigen- cells degranulates.
- Release histamine and pharmacological mediators of anaphylaxis from cell.
- The physiological role of IgE appears to be protection against pathogens by mast cell degranulation and release of inflammatory mediators



Immunoglobulin D (Ig D)

- Structure is similar to IgG
- Serum concentration 30 micrograms per ml
- Constitutes 0.2% of total immunoglobulins
- Half life: 3 days
- IgD together with IgM is major membrane bound immunoglobulin on unstimulated B lymphocytes- acts as recognition receptors for antigens



Thank
you